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<110> Daniel Cohen
Ilya Chumakov

<120> Treatment of CNS Disorders Using D-Amino Acid Oxidase and D-Aspartate Oxidase Antagonists

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 Ile Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val
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 Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp
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 Pro Asn Asn Pro Gln Glu Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr
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 Leu Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser
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 Asp Met Phe Pro Asp Tyr Gly Tyr Gly Trp Phe His Thr Ser Leu Ile
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Thr Val Thr Leu Gly Gly Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu			
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Glu Pro Thr Leu Lys Asn Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe			
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Gly Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe			
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Gly Arg Ile Leu Glu Lys Lys Leu Ser Arg Met Pro Pro Ser His			
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Leu			
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Ile Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val	
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Leu Gln Pro Leu Asp Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu	
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Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp	
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Pro Glu Arg Gly Ile Tyr Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln	
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Gly Pro Ser Asn Thr Glu Val Ile His Asn Tyr			
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Gly Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe			
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Gly Arg Ile Leu Glu Glu Lys Lys Leu Ser Arg Met Pro Pro Ser His			
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Thr	Thr Asp	Val Ala	Ala Gly	Leu Trp	Gln Pro Tyr Leu Ser Asp	
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ccc	aac aac	cca cag	gag gcg	acc ctt	cct gga	365
Pro	Asn Asn	Pro Gln	Glu Ala	Thr Leu	Pro Gly Arg Thr Gln Phe Trp	
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gaaga	atgtca agaattattt	gtgaacgaac	tggctccgg	ccagtagcc	cccagattcg	897
gct	agaaaga gaacagttc	gcaactggacc	ttcaaacaca	gaggcatcc	acaactatgg	957
ccat	gggatc ccatccactg	ggatgtgcc	ctggaggcag	ccaagcttct		1017
tgg	gatc ttcttcc	ttttcc	ttttcc	ttttcc	ttttcc	1077
ccagt	gtactg ccaccc	ttttcc	ttttcc	ttttcc	ttttcc	1137
tgc	ttttcc taagccattt	ttttcc	ttttcc	ttttcc	ttttcc	1197
cct	ttttcc acttcttcc	ttttcc	ttttcc	ttttcc	ttttcc	
tttca	ttttcc taaaagaagc	ttttcc	ttttcc	ttttcc	ttttcc	
aaag	ttttcc aaagtca	ttttcc	ttttcc	ttttcc	ttttcc	1257
aaag	ttttcc cttggagaag	ttttcc	ttttcc	ttttcc	ttttcc	
ccat	ttttcc gtttcagccc	ttttcc	ttttcc	ttttcc	ttttcc	
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ttttcc	ttttcc ccagtgc	ttttcc	ttttcc	ttttcc	ttttcc	

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 Met
 1
 cgt gtg gtg gtg att gga gca gga gtc atc ggg ctg tcc acc gcc ctc 164
 Arg Val Val Val Ile Gly Ala Gly Val Ile Gly Leu Ser Thr Ala Leu
 5 10 15
 tgc atc cat gag cgc tac cac tca gtc ctg cag cca ctg gac ata aag 212
 Cys Ile His Glu Arg Tyr His Ser Val Leu Gln Pro Leu Asp Ile Lys
 20 25 30
 gtc tac gcg gac cgc ttc acc cca ctc acc acc gac gtg gct gcc 260
 Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala Ala
 35 40 45
 ggc ctc tgg cag ccc tac ctt tct gac ccc aac aac cca cag gag gcg 308
 Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu Ala
 50 55 60 65
 gac tgg agc caa cag acc ttt gac tat ctc ctg agc cat gtc cat tct 356
 Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His Ser
 70 75 80
 ccc aac gct gaa aac ctg ggc ctg ttc cta atc tcg ggc tac aac ctc 404
 Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn Leu
 85 90 95
 ttc cat gaa gcc att ccg gtg gca aga gaa ggc gca gac gtg att gtc 452
 Phe His Glu Ala Ile Pro Val Ala Arg Glu Gly Ala Asp Val Ile Val
 100 105 110
 aac tgc act ggg gta tgg gct ggg gcg cta caa cga gac ccc ctg ctg 500
 Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp Pro Leu Leu
 115 120 125
 cag cca ggc cgg ggg cag atc atg aag gtg gac gcc cct tgg atg aag 548
 Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro Trp Met Lys
 130 135 140 145
 cac ttc att ctc acc cat gac cca gag aga ggc atc tac aat tcc ccg 596

His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr Asn Ser Pro			
150	155	160	
tac atc atc cca ggg acc cag aca gtt act ctt gga ggc atc ttc cag			644
Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe Gln			
165	170	175	
ttg gga aac tgg agt gaa cta aac aat atc cag gac cac aac acc att			692
Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr Ile			
180	185	190	
tgg gaa ggc tgc tgc aga ctg gag ccc aca ctg aag aat gca aga att			740
Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg Ile			
195	200	205	
att ggt gaa cga act ggc ttc cgg cca gta cgc ccc cag att cgg cta			788
Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg Leu			
210	215	220	225
gaa aga gaa cag ctt cgc act gga cct tca aac aca gag gtc atc cac			836
Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile His			
230	235	240	
aac tat ggc cat gga ggc tac ggg ctc acc atc cac tgg gga tgt gcc			884
Asn Tyr Gly His Gly Tyr Gly Leu Thr Ile His Trp Gly Cys Ala			
245	250	255	
ctg gag gca gcc aag ctc ttt ggg aga atc ctg gaa gaa aag aaa ttg			932
Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu Lys Lys Leu			
260	265	270	
tcc aga atg cca cca tcc cac ctc tgaagactcc agtgactgct gcctcccc			986
Ser Arg Met Pro Pro Ser His Leu			
275	280		
acaagaactc ccttctcccc tcagccaatg aatcaatgtc ctccttcata agccattgct			1046
tctccctcac ttctttctc aaagaagcat gaggtgagag aaagccacaa agtcagtgcc			1106
tggagaaggg tttagccaa catggggccc ctctcatcac taaaatccct ctaccctctc			1166
tgggtctggc attataaaga acagctgagg ctgtcattcc atgagtcttc agaagaaagg			1226
acagctcaga aaatcaaaga ggccaactgc ccagagccac agaaaatgga ggataattga			1286
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Leu Cys Ile His Glu Arg Tyr His Ser Val Leu Gln Pro Leu Asp Ile			
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala			
35	40	45	
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu			
50	55	60	
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His			
65	70	75	80
Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn			
85	90	95	
Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu			
100	105	110	
Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr			
115	120	125	
Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr			

130	135	140
Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe		
145	150	155
Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp		160
165	170	175
Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp		
180	185	190
Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro		
195	200	205
Trp Met Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr		
210	215	220
Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly		
225	230	235
Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His		240
245	250	255
Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn		
260	265	270
Ala Arg Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln		
275	280	285
Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu		
290	295	300
Val Ile His Asn Tyr Gly His Gly Tyr Gly Leu Thr Ile His Trp		
305	310	315
Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu		320
325	330	335
Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu		
340	345	

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20	25	30
Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala		
35	40	45
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu		
50	55	60
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His		
65	70	75
Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn		80
85	90	95
Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu		
100	105	110
Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr		
115	120	125
Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr		
130	135	140
Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe		
145	150	155
Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp		160
165	170	175
Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp		

180	185	190
Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Asp Pro Asp Ser		
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Tyr Ser Trp Arg His Leu Pro Val Gly Lys Leu Glu		
210	215	220

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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala		
35	40	45
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu		
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Ala Thr Leu Pro Gly Arg Thr Gln Phe Trp Asp Phe Gly Ser		
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala		
35	40	45
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu		
50	55	60
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His		
65	70	75
Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn		
85	90	95
Leu Phe His Glu Ala Ile Pro Val Ala Arg Glu Gly Ala Asp Val Ile		
100	105	110
Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp Pro Leu		
115	120	125
Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro Trp Met		
130	135	140
Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr Asn Ser		
145	150	155
Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe		
165	170	175
Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr		
180	185	190
Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg		
195	200	205
Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg		
210	215	220

Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile
 225 230 235 240
 His Asn Tyr Gly His Gly Tyr Gly Leu Thr Ile His Trp Gly Cys
 245 250 255
 Ala Leu Glu Ala Ala Lys Leu Phe Gly Arg Ile Leu Glu Glu Lys Lys
 260 265 270
 Leu Ser Arg Met Pro Pro Ser His Leu
 275 280

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 attaaaaatag cttgttaggat tactcatttt crtttttctt ctttttaaat ataaagcaat 180
 gtcatcactt tttccctgt attatatttc tcctcaataa ttgatatgct acattaaagg 240
 aacacaaaat ggtcttaatt atgcaataat gatcaaggca aagagtgtt cctggaaact 300
 aatgggtgcc tgagaggagg tggatggcttg aggtccagct ggttattaag ccgcaggaaa 360
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 gtcagggtgt gagatggta cttgataactac attcttcca agctgttgc tgaatcggtt 360
 taagacaaag tcattactag gctgtaaact gttgctctgc aaaattgagc agcacgtatt 420
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Lys Leu Met Gly Ala Asp Xaa Leu Gln Leu Phe Arg Ser Arg Tyr Thr		
5 10 15		
ttg ggt aaa atc tac ttc ata ggt ttt caa arg agc att ctt ctg agc	151	
Leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile Leu Leu Ser		
20 25 30 35		
aaa tct gaa aac tct cta aac tct att gca aag gag aca gaa kaa gga	199	
Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr Glu Xaa Gly		
40 45 50		
aga gag acg gta aca agg aaa gaa rga tgg aag aga agg cat gag gac	247	
Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg His Glu Asp		
55 60 65		
ggc tat ttg gaa atg gca cag agg cat tta cag aga tca tta tgt cct	295	
Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser Leu Cys Pro		
70 75 80		
tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa gaa gta agc	343	
Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu Glu Val Ser		
85 90 95		
agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag ttc ctt gmc	391	
Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu Phe Leu Xaa		
100 105 110 115		
tat gag gcc tct aar gac cgc agg cag cct cta gaa cga atg tgg acc	439	
Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg Met Trp Thr		
120 125 130		

tgc aac tac aac cag caa aaa gac cag tca tgc aac cac aag gaa ata Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His Lys Glu Ile 135 140 145	487
act tct acc aaa gct gaa tgagtttgg a agcagattct tcccccacaa Thr Ser Thr Lys Ala Glu 150	535
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Arg	Tyr	Thr	Leu	Gly	Lys	Ile	Tyr	Phe	Ile	Gly	Phe	Gln	Xaa	Ser	Ile
						20			25				30		
Leu	Leu	Ser	Lys	Ser	Glu	Asn	Ser	Leu	Asn	Ser	Ile	Ala	Lys	Glu	Thr
						35			40			45			
Glu	Xaa	Gly	Arg	Glu	Thr	Val	Thr	Arg	Lys	Glu	Xaa	Trp	Lys	Arg	Arg
						50			55			60			
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						65			70			75			80
Leu	Cys	Pro	Trp	Val	Ser	Tyr	Leu	Pro	Gln	Pro	Tyr	Ala	Glu	Leu	Glu
						85			90			95			
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						100			105			110			
Phe	Leu	Xaa	Tyr	Glu	Ala	Ser	Lys	Asp	Arg	Arg	Gln	Pro	Leu	Glu	Arg
						115			120			125			
Met	Trp	Thr	Cys	Asn	Tyr	Asn	Gln	Gln	Lys	Asp	Gln	Ser	Cys	Asn	His
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<212> DNA
<213> *Homo sapiens*

cat gag gac ggc tat ttg gaa atg gca cag agg cat tta cag aga tca His Glu Asp Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser 1 5 10 15 tta tgt cct tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu 20 25 30 gaa gta agc agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu 35 40 45 ttc ctt gcc tat gag gcc tct aag gac cgc agg cag cct cta gaa cga Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg 50 55 60 atg tgg acc tgc aac tac aac cag caa aaa gac cag tca tgc aac cac Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His 65 70 75 80 aag gaa ata act tct acc aaa gct gaa tgagtttggaa agcagattct Lys Glu Ile Thr Ser Thr Lys Ala Glu 85 tccccagccaa tccttctgtat gacaatgttag tctggccaac atcttcactg gactctgacg	48 96 144 192 240 287 347
---	---

gactctgtgt ctgggaccca gctgataaca cgtggatgtg ggattgtatt tgcaactctc	407
tggtcagtaa gtgataaaat gccatttcta tgcacccacc tggctgtgt gactggaga	467
atctcttt	476

<210> 16
<211> 89
<212> PRT
<213> Homo sapiens

<400> 16

His Glu Asp Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser	
1 5 10 15	
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu	
20 25 30	
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu	
35 40 45	
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg	
50 55 60	
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His	
65 70 75 80	
Lys Glu Ile Thr Ser Thr Lys Ala Glu	
85	

<210> 17
<211> 1633
<212> DNA
<213> Homo sapiens

<400> 17

ttgggttcca ttgcaacccg aggcgagact agagttccca agcgagaagg gaagaggcag	60
tgggtgcacg tggaaaggcgg acagaggcgct ggaaacaaga cgctccagaa tcaggagctt	120
cccttcagga aatagcatcc tgggtccccg cactgcagtt gtctggtctc tccagcagtt	180
tggtaacttcc ggctgctgca atg cgt gtg gtg att gga gca gga gtc atc	233
Met Arg Val Val Val Ile Gly Ala Gly Val Ile	
1 5 10	
ggg ctg tcc acc gcc ctc tgc atc cat gag cgc tac cac tca gtc ctg	281
Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val Leu	
15 20 25	
cag cca ctg cac ata aag gtc tac gcg gac cgc ttc acc cca ctc acc	329
Gln Pro Leu His Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr	
30 35 40	
acc acc gac gtg gct gcc ggc ctc tgg cag ccc tac ctt tct gac ccc	377
Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro	
45 50 55	
aac aac cca cag gag gcg gac tgg agc caa cag acc ttt gac tat ctc	425
Asn Asn Pro Gln Glu Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu	
60 65 70 75	
ctg agc cat gtc cat tct ccc aac gct gaa aac ctg ggc ctg ttc cta	473
Leu Ser His Val His Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu	
80 85 90	
atc tcg ggc tac aac ctc ttc cat gaa gcc att ccg gac cct tcc tgg	521
Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp	
95 100 105	
aag gac aca gtt ctg gga ttt cgg aag ctg acc ccc aga gag ctg gat	569
Lys Asp Thr Val Leu Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp	
110 115 120	
atg ttc cca gat tac ggc tat ggc tgg ttc cac aca agc cta att ctg	617

Met Phe Pro Asp Tyr Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu			
125	130	135	
gag gga aag aac tat cta cag tgg ctg act gaa agg tta act gag agg			665
Glu Gly Lys Asn Tyr Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg			
140	145	150	155
gga gtg aag ttc ttc cag cgg aaa gtg gag tct ttt gag gag gtg gca			713
Gly Val Lys Phe Phe Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala			
160	165	170	
aga gaa ggc gca gac gtg att gtc aac tgc act ggg gta tgg gct ggg			761
Arg Glu Gly Ala Asp Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly			
175	180	185	
gcg cta caa cga gac ccc ctg ctg cag cca ggc cgg ggg cag atc atg			809
Ala Leu Gln Arg Asp Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met			
190	195	200	
aag gtg gac gcc cct tgg atg aag cac ttc att ctc acc cat gac cca			857
Lys Val Asp Ala Pro Trp Met Lys His Phe Ile Leu Thr His Asp Pro			
205	210	215	
gag aga ggc atc tac aat tcc ccg tac atc atc cca ggg acc cag aca			905
Glu Arg Gly Ile Tyr Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr			
220	225	230	235
gtt act ctt gga ggc atc ttc cag ttg gga aac tgg agt gaa cta aac			953
Val Thr Leu Gly Gly Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn			
240	245	250	
aat atc cag gac cac aac acc att tgg gaa ggc tgc tgc aga ctg gag			1001
Asn Ile Gln Asp His Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu			
255	260	265	
ccc aca ctg aag aat gca aga att att ggt gaa gca act ggc ttc cgg			1049
Pro Thr Leu Lys Asn Ala Arg Ile Ile Gly Glu Ala Thr Gly Phe Arg			
270	275	280	
cca gta cgc ccc cag att cggt cta gaa aga gaa cag ctt cgc act gga			1097
Pro Val Arg Pro Gln Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly			
285	290	295	
cct tca aac aca gag gtc atc cac aac tat ggc cat gga ggc tac ggg			1145
Pro Ser Asn Thr Glu Val Ile His Asn Tyr Gly His Gly Tyr Gly			
300	305	310	315
ctc acc atc cac tgg gga tgt gcc ctg gag gca gcc aag ctc ttt ggg			1193
Leu Thr Ile His Trp Gly Cys Ala Leu Glu Ala Ala Lys Leu Phe Gly			
320	325	330	
aga atc ctg gaa gaa aag aaa ttg tcc aga atg cca cca tcc cac ctc			1241
Arg Ile Leu Glu Glu Lys Lys Leu Ser Arg Met Pro Pro Ser His Leu			
335	340	345	
tgaagactcc agtgactgct gcctcccccc acaaactc ccttctcccc tcagccaatg			1301
aatcaatgtc ctccttcata agccattgct tctccctcac ttcttcctc aaagaagcat			1361
gaggtgagag aaagccacra agtcagtgcc tggagaaggg ttccagccaa catggggccc			1421
ctctcatcac tggaaatccct ctaccttctc tgggtctggc attataaaga acagctgagg			1481
ctgtcattcc atgagtcctc agaagaaaagg acagctcaga aagtcaaaga ggccaactgc			1541
ccagagccac agaaaaatgga ggataattga ggctaagtaa cctgattaca agttgtacta			1601
acatattaaa ggttctgaaa agtcctgcaa aa			1633

<210> 18

<211> 347

<212> PRT

<213> Homo sapiens

<400> 18

Met Arg Val Val Val Ile Gly Ala Gly Val Ile Gly Leu Ser Thr Ala

1	5	10	15												
Leu	Cys	Ile	His	Glu	Arg	Tyr	His	Ser	Val	Leu	Gln	Pro	Leu	Asp	Ile
20	25	30													
Lys	Val	Tyr	Ala	Asp	Arg	Phe	Thr	Pro	Leu	Thr	Thr	Thr	Asp	Val	Ala
35	40	45													
Ala	Gly	Leu	Trp	Gln	Pro	Tyr	Leu	Ser	Asp	Pro	Asn	Asn	Pro	Gln	Glu
50	55	60													
Ala	Asp	Trp	Ser	Gln	Gln	Thr	Phe	Asp	Tyr	Leu	Leu	Ser	His	Val	His
65	70	75	80												
Ser	Pro	Asn	Ala	Glu	Asn	Leu	Gly	Leu	Phe	Leu	Ile	Ser	Gly	Tyr	Asn
85	90	95													
Leu	Phe	His	Glu	Ala	Ile	Pro	Asp	Pro	Ser	Trp	Lys	Asp	Thr	Val	Leu
100	105	110													
Gly	Phe	Arg	Lys	Leu	Thr	Pro	Arg	Glu	Leu	Asp	Met	Phe	Pro	Asp	Tyr
115	120	125													
Gly	Tyr	Gly	Trp	Phe	His	Thr	Ser	Leu	Ile	Leu	Glu	Gly	Lys	Asn	Tyr
130	135	140													
Leu	Gln	Trp	Leu	Thr	Glu	Arg	Leu	Thr	Glu	Arg	Gly	Val	Lys	Phe	Phe
145	150	155	160												
Gln	Arg	Lys	Val	Glu	Ser	Phe	Glu	Glu	Val	Ala	Arg	Glu	Gly	Ala	Asp
165	170	175													
Val	Ile	Val	Asn	Cys	Thr	Gly	Val	Trp	Ala	Gly	Ala	Leu	Gln	Arg	Asp
180	185	190													
Pro	Leu	Leu	Gln	Pro	Gly	Arg	Gly	Gln	Ile	Met	Lys	Val	Asp	Ala	Pro
195	200	205													
Trp	Met	Lys	His	Phe	Ile	Leu	Thr	His	Asp	Pro	Glu	Arg	Gly	Ile	Tyr
210	215	220													
Asn	Ser	Pro	Tyr	Ile	Ile	Pro	Gly	Thr	Gln	Thr	Val	Thr	Leu	Gly	Gly
225	230	235	240												
Ile	Phe	Gln	Leu	Gly	Asn	Trp	Ser	Glu	Leu	Asn	Asn	Ile	Gln	Asp	His
245	250	255													
Asn	Thr	Ile	Trp	Glu	Gly	Cys	Cys	Arg	Leu	Glu	Pro	Thr	Leu	Lys	Asn
260	265	270													
Ala	Arg	Ile	Ile	Gly	Glu	Ala	Thr	Gly	Phe	Arg	Pro	Val	Arg	Pro	Gln
275	280	285													
Ile	Arg	Leu	Glu	Arg	Glu	Gln	Leu	Arg	Thr	Gly	Pro	Ser	Asn	Thr	Glu
290	295	300													
Val	Ile	His	Asn	Tyr	Gly	His	Gly	Gly	Tyr	Gly	Leu	Thr	Ile	His	Trp
305	310	315	320												
Gly	Cys	Ala	Leu	Glu	Ala	Ala	Lys	Leu	Phe	Gly	Arg	Ile	Leu	Glu	Glu
325	330	335													
Lys	Lys	Leu	Ser	Arg	Met	Pro	Pro	Ser	His	Leu					
340	345														

<210> 19
<211> 1200
<212> DNA
<213> Homo sapiens

<400> 19	
atg gac aca gca cgg att gca gtt gtc ggg gca ggt gtg gtg ggg ctc	48
Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu	
1 5 10 15	
tcc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc	96
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr	
20 25 30	
atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc	144

Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala			
35	40	45	
gga atg ctt att cct cac act tat cca gat aca ccc att cac acg cag			192
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln			
50	55	60	
aag cag tgg ttc aga gaa acc ttt aat cac ctc ttt gca att gcc aat			240
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn			
65	70	75	80
tct gca gaa gct gga gat gct ggt gtt cat ttg gta tca ggt tgg cag			288
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln			
85	90	95	
ata ttt cag agc act ccg act gaa gaa gtg cca ttc tgg gct gac gtg			336
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val			
100	105	110	
gtt ctg gga ttt cga aag atg act gag gct gag ctg aag aaa ttc ccc			384
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro			
115	120	125	
cag tat gtg ttt ggt cag gct ttt aca acc ctg aaa tgt gaa tgc cct			432
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro			
130	135	140	
gcc tac ctc ccg tgg ttg gag aaa agg ata aag gga agt gga ggc tgg			480
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp			
145	150	155	160
aca ctc act ccg cga ata gaa gac ctg tgg gaa ctt cat ccg tcc ttt			528
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe			
165	170	175	
gac atc gtg gtc aac tgt tca ggc ctt gga agc aga cag ctt gca gga			576
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly			
180	185	190	
gac tca aag att ttc cct gta agg ggc caa gtc ctc caa gtt cag gct			624
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala			
195	200	205	
ccc tgg gtg gag cat ttt atc cga gat ggc agt ggg ctg aca tat att			672
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile			
210	215	220	
tat cct ggt aca tcc cat gta acc cta ggt gga act agg caa aaa ggg			720
Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly			
225	230	235	240
gac tgg aat ctg tcc ccg gat gca gaa aat agc aga gag att ctt tcc			768
Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser			
245	250	255	
cga tgc tgt gct ctg gag ccc tcc ctc cac gga gcc tgc aac atc agg			816
Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly Ala Cys Asn Ile Arg			
260	265	270	
gag aag gtg ggc ttg agg ccc tac agg cca ggc gtg cga ctg cag aca			864
Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr			
275	280	285	
gag ctc ctt gcg cga gat gga cag agg ctg cct gta gtc cac cac tat			912
Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr			
290	295	300	
ggc cat ggg agt ggg ggc atc tca gtg cac tgg ggc act gct ctg gag			960
Gly His Gly Ser Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu			
305	310	315	320
gcc gcc agg ctg gtg agc gag tgt gtc cat gcc ctc agg acc ccc att			1008
Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile			
325	330	335	
ccc aag tca aac ctg tagatgacat aaaatgacag caaagagact gagagactgt			1063

Pro Lys Ser Asn Leu

340

tgatcaaagc acagaacagg ttcaaaataac ttttccactg catgaaagtt taatttagaca
tttctttgtt ttcaacatta gaagtgggt aacatgtaa ctgagcacgg tagcatgcct
atagtcccag ctacttg

1123

1183

1200

<210> 20

<211> 1023

<212> DNA

<213> Homo sapiens

<400> 20

atg gac aca gca cgg att gca gtt gtc ggg gca ggt gtg gtg ggg ctc
Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu

5 10 15

tcc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr

20 25 30

atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Ser Asp Val Ala Ala

35 40 45

gga atg ctt att cct cac act tat cca gat aca ccc att cac acg cag
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln

50 55 60

aag cag tgg ttc aga gaa acc ttt aat cac ctc ttt gca att gcc aat
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn

65 70 75 80

tct gca gaa gct gga gat gct ggt gtt cat ttg gta tca ggg ata aag
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys

85 90 95

gga agt gga ggc tgg aca ctc act cgg cga ata gaa gac ctg tgg gaa
Gly Ser Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu

100 105 110

ctt cat ccg tcc ttt gac atc gtc aac tgt tca ggc ctt gga agc
Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser

115 120 125

aga cag ctt gca gga gac tca aag att ttc cct gta agg ggc caa gtc
Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val

130 135 140

ctc caa gtt cag ccc tgg gtg gag cat ttt atc cga gat ggc agt
Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser

145 150 155 160

ggg ctg aca tat att tat cct ggt aca tcc cat gta acc cta ggt gga
Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly

165 170 175

act agg caa aaa ggg gac tgg aat ctg tcc ccg gat gca gaa aat agc
Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser

180 185 190

aga gag att ctt tcc cga tgc tgt gct ctg gag ccc tcc ctc cac gga
Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly

195 200 205

gcc tgc aac atc agg gag aag gtg ggc ttg agg ccc tac agg cca ggc
Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly

210 215 220

gtg cga ctg cag aca gag ctc ctt gcg cga gat gga cag agg ctg cct
Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro

225 230 235 240

gta gtc cac cac tat ggc cat ggg agt ggg ggc atc tca gtg cac tgg	768
Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp	
245 250 255	
ggc act gct ctg gag gcc gcc agg ctg gtg agc gag tgt gtc cat gcc	816
Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala	
260 265 270	
ctc agg acc ccc att ccc aag tca aac ctg tagatgacat aaaatgacag	866
Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu	
275 280	
caaagagact gagagactgt tgatcaaagg acagaacagg ttcaaataac tttccactg	926
catgaaaagtt taatttagaca tttctttgtt ttcaacatta gaagtggtgt aacatgtaa	986
ctgagcacgg tagcatgcct atagtcccag ctacttg	1023

<210> 21

<211> 341

<212> PRT

<213> Homo sapiens

<400> 21

Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu	
1 5 10 15	
Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr	
20 25 30	
Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala	
35 40 45	
Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln	
50 55 60	
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn	
65 70 75 80	
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln	
85 90 95	
Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val	
100 105 110	
Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro	
115 120 125	
Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro	
130 135 140	
Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp	
145 150 155 160	
Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe	
165 170 175	
Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly	
180 185 190	
Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala	
195 200 205	
Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile	
210 215 220	
Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly	
225 230 235 240	
Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser	
245 250 255	
Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly Ala Cys Asn Ile Arg	
260 265 270	
Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr	
275 280 285	
Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr	
290 295 300	

Gly His Gly Ser Gly Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu
 305 310 315 320
 Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile
 325 330 335
 Pro Lys Ser Asn Leu
 340

<210> 22

<211> 282

<212> PRT

<213> Homo sapiens

<400> 22

Met Asp Thr Ala Arg Ile Ala Val Val Gly Ala Gly Val Val Gly Leu
 1 5 10 15
 Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr
 20 25 30
 Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala
 35 40 45
 Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln
 50 55 60
 Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn
 65 70 75 80
 Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys
 85 90 95
 Gly Ser Gly Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu
 100 105 110
 Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser
 115 120 125
 Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val
 130 135 140
 Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser
 145 150 155 160
 Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly
 165 170 175
 Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser
 180 185 190
 Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly
 195 200 205
 Ala Cys Asn Ile Arg Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly
 210 215 220
 Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro
 225 230 235 240
 Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp
 245 250 255
 Gly Thr Ala Leu Glu Ala Ala Arg Leu Val Ser Glu Cys Val His Ala
 260 265 270
 Leu Arg Thr Pro Ile Pro Lys Ser Asn Leu
 275 280

<210> 23

<211> 47

<212> DNA

<213> Artificial Sequence

<220>

<223> oligonucleotide 24-1443-126

<220>
 <221> allele
 <222> 24
 <223> polymorphic base C or T

 <400> 23
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<210> 24
 <211> 47
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> oligonucleotide 24-1457-52

<220>
 <221> allele
 <222> 24
 <223> polymorphic base C or A

 <400> 24
 tctgagatgc ccctgtgtcc tctmagggag tagtggctga gcatttc 47

<210> 25
 <211> 47
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> oligonucleotide 27-93-181

<220>
 <221> allele
 <222> 24
 <223> polymorphic base C or T

 <400> 25
 cccagctctg ccactggcga gctytgtggc cttggcaag ttactcc 47

<210> 26
 <211> 47
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> oligonucleotide 24-1461-256

<220>
 <221> allele
 <222> 24
 <223> polymorphic base A or G

 <400> 26
 gatggctctg gcattttcag ggarcagtca tgtctgatct caagtcc 47